Outcome of lower-extremity revascularization in patients younger than 40 years in a predominately diabetic population

Stephanie S. Saltzberg, MD, Frank B. Pomposelli, Jr, MD, Alana K. Belfield, BA, Malachi G. Sheahan, MD, David R. Campbell, MD, John J. Skillman, MD, Frank W. LoGerfo, MD, and **Allen D. Hamdan, MD,** *Boston, Mass*

Objective: **Incidence of perioperative complications is increased and outcome is poor in young patients undergoing vascular surgery. We extensively reviewed results of lower-extremity procedures in this group of patients to further define the extent of short-term and long-term morbidity.**

Methods: **Results from our vascular registry were retrospectively reviewed for 76 lower-extremity revascularization procedures performed between January 1990 and May 2000 in 51 patients younger than 40 years. This represents 1.88% of 4052 lower-extremity bypass procedures performed during this period. Perioperative cardiac complications, long-term survival, graft patency, and limb salvage were evaluated. Kaplan-Meier curves were generated, and their significance was determined with the Cox-Mantel test.**

Results: **Forty-nine percent of patients were male, and 51% were female; mean age at presentation was 35.9 years (range, 27.5-39.8 years). Preoperative morbidity included diabetes mellitus (96.1%), smoking (70.6%), hypertension (78.4%), coronary artery disease (37.3%), hyperlipidemia (33.3%), and renal dysfunction (52.9%). Overall rate for 30-day postoperative mortality was 0.0%, for myocardial infarction was 0.0%, and for congestive heart failure was 1.32%. Thirty-day graft failure was 11.1% (n = 9). At 1 year, primary patency was 71.0%, secondary patency was 82.5%, and limb salvage was 87.1%; and at 5 years these rates were 51.9%, 63.4%, and 77.2%, respectively. After the initial surgery 11.8% (n = 6) of patients required at least one additional ipsilateral revascularization procedure, 31.3% (n = 16) required a bypass graft in the contralateral limb, and 23.5% (n = 12) ultimately required amputation. In patients who required additional ipsilateral procedures, 1-year primary patency rate was 66.7%, secondary patency rate was 62.5%, and limb salvage rate was 77.8%, compared with 5-year rates of 44.4%, 41.7%, and 64.8%, respectively, representing a decrease in patency compared with primary revascularization procedures. Overall survival at 1 year was 88.2%, compared with 73.3% at 5 years. Patients with preexisting renal disease had significantly decreased survival at 5 years compared with those without renal dysfunction (64.5% vs 82.6%; *P* = .019).**

Conclusions: **Our data suggest that age younger than 40 years is not associated with increased perioperative morbidity and mortality. However, these patients have a significant rate of early graft failure and dismal long-term survival, especially in patients with preexisting renal dysfunction. In addition, ipsilateral repeat operations have a marginal success rate. (J Vasc Surg 2003;38:1056-9.)**

Arterial occlusive disease in young patients is rare but complex.[1,2] The incidence of atherosclerosis in young patients ranges from 1.4% to 17%.[3]

Premature atherosclerosis is the most common cause of lower-extremity ischemia in young adults.[1] This form of atherosclerosis, unlike that in elderly patients, is considered an aggressive disease with rapid progression and poor prognosis.[1,4-10]

The cause of premature atherosclerosis is unclear. Several factors have been identified that may increase risk for accelerated atherosclerosis in young patients. Smoking, hypercoagulable states, and renal failure are considered significant risk factors for development of the disease.[1,3,5,7,9,10] In addition, patients with type I diabetes mellitus are at increased risk for lower extremity ischemia early in life.[3,11,12] Type I diabetes is also associated with significantly increased mortality. Data from the Joslin Diabetes Center demonstrate a mortality rate of 50% in patients with type I diabetes by age 54 years, and a median 25-year decrease in survival compared with the general population.[11]

Controversy has surrounded lower extremity revascularization in young patients.[1,4,8,12] Increased perioperative complications and poor outcome has been reported in young patients undergoing vascular surgery.[1,9,10,13,14] Levy et al[1] demonstrated that in patients younger than 40 years requiring lower-extremity bypass grafting the rate of secondary procedures was 53% and the amputation rate was 27%. The increased rate of multiple revascularization procedures and progression to amputation are consistent with findings of other studies. Toursarkissian et al[15] demonstrated an 18-month primary patency rate of 60% ± 11% and a limb salvage rate of 71% ± 9% in patients younger than 50 years. In addition, 5-year mortality in these young

From the Division of Vascular Surgery, Beth Israel Deaconess Medical Center, West Campus, Harvard Medical School.

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Reprint requests: Allen D. Hamdan, MD, Division of Vascular Surgery, Beth Israel Deaconess Medical Center, West Campus, 110 Francis St, Ste 5B, Boston, MA 02215 (e-mail: ahamdan@caregroup.harvard.edu).

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Table I. Clinical characteristics of patient population

Characteristic	*Percent of patients*
Gender	
Male	49
Female	51
Diabetes mellitus	
Type I	94.1
Type II	2.0
Comorbid condition	
Hypertension	78.4
Coronary artery disease	37.3
Hyperlipidemia	33.3
Cerebrovascular disease	9.8
Previous congestive heart failure	15.7
Previous myocardial infarction	21.6
Smoking (past or present)	70.6
Renal dysfunction*	52.9
Hemodialysis	17.6
Peritoneal dialysis	11.8

Hemodialysis, peritoneal dialysis, creatinine concentration >2.0.

Table II. Conduit used in revascularization procedures

Conduit	*%*
Greater saphenous vein	87
Lesser saphenous vein	1
Arm vein	6
Composite graft	1
Prosthetic graft	5

patients is as high as 17% to 26%.[8,9] Fewer reports have demonstrated that there is no significant difference in outcome for this subgroup of patients.[2,3] In an attempt to more clearly understand the outcome of surgical intervention in these young patients, we report our experience with lower-extremity revascularization in patients younger than 40 years. Almost this entire cohort of young patients undergoing vascular surgery had type I diabetes mellitus.

PATIENTS AND METHODS

We reviewed data for all patients younger than 40 years who underwent lower-extremity revascularization between January 1990 and May 2000 at the West Campus of the Beth Israel Deaconess Medical Center, Boston, Mass. Data were prospectively entered into a computerized vascular registry established in 1990. For patients with multiple operations, risk factors and operative results were entered into the registry for each procedure performed. Staff vascular surgeons with vascular fellows or general surgery residents performed 76 procedures in 51 patients. This represents 1.88% of 4052 lower-extremity bypass graft operations performed during this period. Patients routinely recovered in a vascular step-down unit before being transferred to the patient floor.

Demographic data and preoperative risk factors in our patient population, including age, hypertension, previous myocardial infarction, congestive heart failure, chronic renal insufficiency, and diabetes mellitus, were also entered into the registry. We do not routinely collect laboratory data, such as homocysteine and cholesterol concentrations or results of hypercoagulable workup studies, in our database. Given our institution's affiliation with the Joslin Diabetes Center, our patient population consisted almost exclusively of patients with type I diabetes mellitus. Renal dysfunction included patients with creatinine concentration greater than 2.0, patients receiving hemodialysis or peritoneal dialysis, or patients who had received a kidney transplant.

All patients underwent preoperative angiography, but not all of data were available in the database. Intraoperatively, our standard is to perform continuous hand-held Doppler scanning of the graft. Intraoperative duplex scanning is not performed. Completion angiography is performed sporadically, at the discretion of the surgeon. Angioscopy of all vein conduits is routine.

Postoperative complications, including myocardial infarction and congestive heart failure, were identified at clinical assessment and entered into the registry by staff, residents, or fellows. Routine cycling of cardiac enzymes or postoperative electrocardiography were not performed without clinical indication.

There is no standard protocol for graft surveillance at our institution. Patients with subcutaneous distal grafts undergo hand-held Doppler scanning of the graft at routine office visits. More recently, graft surveillance is being done in more patients.

We were able to obtain the date of death for deceased patients from the Social Security Death Index database and data from our registry. The cause of death was not always identified.

Statistical analysis was performed with StatView software (Version 5.0; SAS Institute, Cary, NC). Independent predictors of postoperative outcome were evaluated with logistic regression analysis. Variables were considered significant at $P < .05$ (Wald test) and if the 95% confidence interval of the odds ratio did not contain the integer 1. Survival analysis was performed with the Kaplan-Meier method, and values were considered significant at $P < .05$ (Cox-Mantel log-rank test).

RESULTS

Forty-nine percent of patients were men, and 51% were women; mean age at presentation was 35.9 years (range, 27.5-39.8 years). Preoperative demographic data (Table I) included diabetes mellitus (96.1%), smoking (70.6%), hypertension (78.4%), coronary artery disease (37.3%), hyperlipidemia (33.3%), and renal dysfunction (52.9%). Of patients with renal dysfunction, 9 were receiving hemodialysis, 6 were receiving peritoneal dialysis, and 9 had received a kidney transplant. The indications for the initial procedure performed at our institution included tissue loss (85.5%), rest pain (9.2%), and claudication (3.9%). Conduit was primarily saphenous vein, with small percentages of arm vein, composite graft, and prosthetic graft (Table II).

Table III. Inflow and outflow vessels used in 76 procedures

Inflow vessel	*n*	*%*	*Outflow vessel*	*n*	*%*
Femoral artery	51	67.1	Dorsalis Pedis artery	23	30.3
Below-knee popliteal artery	16	21.1	Below-knee popliteal artery	18	23.7
Above-knee popliteal artery	6	7.9	Tibial artery	14	18.4
Common iliac artery	2	2.6	Above-knee popliteal artery	9	11.8
Tibial artery	1	1.3	Other	6	7.9
			Femoral artery	3	3.9
			Peroneal artery	3	3.9

Table IV. Patency, limb salvage, and survival rates at 1 and 5 Years

Revascularization outcome and overall survival	*1 y*	*5 y*
Primary procedure		
Primary patency (%)	71.0	51.9
Secondary patency (%)	82.5	63.4
Limb salvage (%)	87.1	77.2
Additional ipsilateral procedures		
Primary patency	66.7	44.4
Secondary patency	62.5	41.7
Limb salvage	77.8	64.8
Overall survival (%)	88.2	73.3

Inflow and outflow vessels are listed in Table III.

Overall 30-day postoperative mortality rate was 0.0%. Thirty-day postoperative myocardial infarction rate was 0.0%, and congestive heart failure rate was 1.32%. Thirty-day graft failure rate was 11.1% (9 of 76 patients). For primary revascularization procedures at 1 year, overall primary patency rate was 71.0%, secondary patency rate was 82.5%, and limb salvage rate was 87.1%; and at 5 years was 51.9%, 63.4%, and 77.2%, respectively (Table IV).

After the initial surgery 11.8% of patients (6 of 51) required at least one additional ipsilateral revascularization procedure. For those requiring additional ipsilateral procedures, at 1 year the primary patency rate was 66.7%, secondary patency rate was 62.5%, and limb salvage was 77.8%; and at 5 years was 44.4%, 41.7%, and 64.8%, respectively (Table 4). Compared with primary revascularization procedures, additional ipsilateral procedures resulted in decreased patency and limb salvage. In addition, 31.3% of patients (16 of 51) required a bypass graft in the contralateral limb, and 23.5% of patients (12 of 51) ultimately required amputation.

Overall survival in this cohort of patients at 1 year was 88.2%, and at 5 years was 73.3%. Patients with preexisting renal dysfunction (27 of 51) had significantly decreased survival at 5 years compared with those with normal renal function (64.5% vs 82.6%; $P = .019$; Fig).

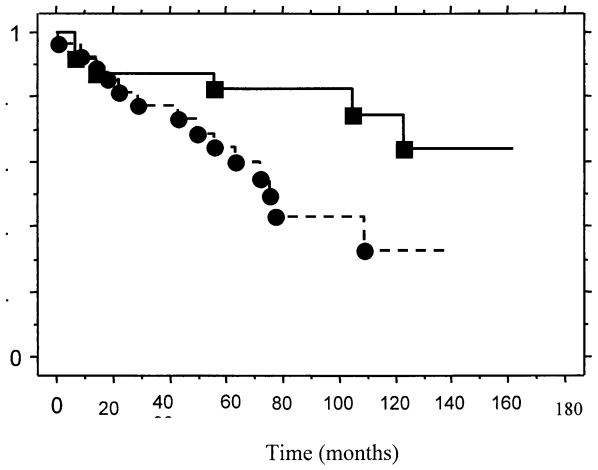
CONCLUSION

Our data suggest that perioperative morbidity and mortality are not increased in patients with diabetes undergoing lower-extremity bypass grafting. In this series there were no perioperative deaths, and overall cardiac morbidity was 1.3%. Our patient population is notable for a high incidence of type I diabetes. This group of patients may not be comparable with young patients with premature atherosclerosis. These findings correlate with recent work from our institution in more than 4000 patients and a study by Kwolek et al,[11] which reported on patients with juvenile-onset diabetes mellitus who underwent revascularization.

Early (30-day) graft failure rate was 11.1%. The specific reasons for this high rate are not clear, but it may reflect more diffuse disease in this group, and a more aggressive approach in younger patients. We may attempt revascularization in patients with suboptimal target vessels. It is difficult to predict in which patients revascularization will fail, and even more difficult to perform primary amputation in a young person without an attempt at revascularization, even if there is risk for failure.

At follow-up we found that 11.8% of patients required at least one additional ipsilateral revascularization procedure, 31.3% required a contralateral bypass graft, and in 23.5% amputation was ultimately necessary. This is potentially important information for patients without primary saphenous vein for whom decisions regarding alternative conduits must be made. Several investigators have found similar decreases in patency and limb salvage.[1,9,10,13,14] Toursarkissian et al[15] evaluated 31 patients younger than 50 years who had diabetes and were undergoing infrainguinal bypass grafting for limb salvage. They also found an acceptable rate of major complications, with comparable limb salvage rates. Harris et al[9] found that patients younger than 50 years with peripheral vascular disease had significantly higher rates of repeat operation, limb salvage, and amputation. In addition, Levy et al[1] reported that patients younger than 40 years frequently had failure of primary arterial reconstructions, need for repeat procedures, and high amputation rates. Both of these reports demonstrated a much lower incidence of diabetes mellitus in their populations of young patients, 35% and 25%, respectively. It is important to differentiate young patients with diabetes from those with premature atherosclerosis in the general population, because of different risk factors.

Our amputation rate of 23.5% correlates with other studies that reported amputation rates ranging from 20.7% to 31% in patients younger than 50 years.[1,4,9] One study found this to be a threefold increase when comparing patients younger and older than 50 years.[4]



Cumulative survival (%) in patients with normal renal function *(squares)* and with renal dysfunction *(circles)*.

In addition, ipsilateral repeat operations were frequently required in these young patients. Success rate was marginal compared with the primary procedure. Primary patency rate, secondary patency rate, and limb salvage rate were 66.7%, 62.5%, 77.8%, respectively, at 1 year and 44.4%, 41.7%, and 64.8%, respectively, at 5 years. The reasons for these results, other than need for alternative conduit, are unclear. Although some studies question the virulence of atherosclerosis in young patients, we believe our findings reflect rapid progression of the disease. We do not, however, perform routine graft surveillance in our patients.

Finally, although we clearly show that these young patients have the same rate of serious perioperative complications as our older patients do, this group had dismal long-term survival, especially those with pre-existing renal dysfunction. Approximately 25% of our patients younger than 40 years did not survive 5 years. The reason for poor long-term survival is unclear, because the cause of death was not known for all patients. However, it can be extrapolated that the complications of diabetes and renal failure may have had a significant role. This is consistent with a previous report from our institution of 145 dialysis-dependent patients with 1-year, 3-year, and 5-year survival rates of 57%, 17%, and 4%, respectively. However, we were unable to clearly identify specific preoperative risk factors that were independent predictors of poor outcome, graft patency, and limb salvage, given the small number of young patients undergoing vascular surgery.

In conclusion, it appears that in patients with diabetes who are younger than 40 years of age, lower-extremity revascularization can be performed with acceptable morbidity and mortality and with reasonable expectation of limb salvage. However, the rate of early graft failure is significant and long-term survival rate is dismal, especially in patients with preexisting renal dysfunction. Multiple attempts after failed primary revascularization are likely to yield inferior results. Young patients need to be made aware of this increased risk for poor outcome, including limb loss, and attempts must be made to mitigate any risk factors to aid longer survival.

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